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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/028,514	02/23/1998	STEPHEN F. GORFIEN	0942.4110002	4800

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
WARE, DEBORAH K	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/028,514	GORFIEN ET AL.	
	Examiner	Art Unit	
	Deborah K. Ware	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 12/29/03.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-3, 6-17, 20-24, 27-37, 73-77, 79-82, 106-109, 112, 140, 143-174 is/are pending in the application.

4a) Of the above claim(s) 79-82, 106-109, 112, 143-153 & 155-174 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3, 6-17, 20-24, 27-37, 73-77, 140, 154 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 6-17, 20-24, 27-37, 73-77, 79-82, 106-109, 112, 140 and 143-174 are pending.

In view of the appeal brief and arguments therewith filed on December 29, 2003, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claims 79-82, 106-109, 112, 143-153, 155 and 156 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention(s) and for reasons of record, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

Claim 1-3, 6-17, 20-24, 27-37, 73-77, 140, 154, and 157-174 are examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-17, 20-22, 27-37, 73-77, 140, 154, 158 and 162 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polyanionic compound which is a polysulfonated or polysulfated compound as in claim 2, and for the use of a serum free or protein free medium, does not reasonably provide enablement for a polycationic compound or other polyanionic compound, and for a medium that is not serum or protein free. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice and carry out the invention commensurate in scope with these claims. The exemplifed disclosure only enables a polysulfonated or polysulfated polyanionic compound and a serum or protein free medium. There is no disclosure in the specfication as to how one of skill in the art would practice the claimed invention using a polycationic compound or another polyanionic compound and a medium that is not serum or protein free. There would be a high degree of unpredictability in this art to carry out the claimed method *for any mammalian cell type* using a polycationic compound since there are no examples disclosed in the instant specification to demonstrate that the same can be performed with any predictable positive outcome for viable cell recovery. Therefore, there would be an undue burden of experimentation placed upon one of skill in this art to carry out the claimed invention. The claims are not considered to be enabled for the scope as claimed and should be limited to the enabling instant disclosure which appears to be directed to polyanionic compounds and no

disclosure is evident in the instant specification regarding cationic compounds, or any polyanionic compound and for a medium that is not serum or protein free.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by **newly cited** Mignot et al.

Claims are drawn to a method of cultivating a mammalian cell in suspension comprising obtaining a mammalian cell to be cultivated and contacting the cell with a serum free cell culture medium comprising at least one polyanionic or polycationic compound. Further, the polyanionic compound is a polysulfonated compound or a polysulfated compound. The polysufonated or polysulfated compound is selected from the group consisting of heparin, heparin sulfate, chondroitin sulfate, derma tan sulfate, pentosan sulfate and a proteoglycan.

Mignot et al teach a method of cultivating a mammalian cell in suspension comprising obtaining a mammalian cell to be cultivated and contacting the cell with a

serum free cell culture medium comprising at least one polyanionic or polycationic compound. Further, the polyanionic compound is a polysulfonated compound or a polysulfated compound. The polysufonated or polysulfated compound is selected from the group consisting of heparin, heparin sulfate, and dermatan sulfate. Note the abstract and col. 2, lines 30-31 and line 40 and lines 44-46.

The claims are identical to the claimed subject matter and are therefore, considered to be anticipated by the teachings therein. Although it is noted that Mignot et al does teach that their culture medium can contain alternatively a dextran sulfate it does not have to contain dextran sulfate and does teach a medium which does not contain dextran sulfate. Thus, the claims are identical to the teachings therein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-14, 22-24, 27-32, 35-37, 140, 154, and 157-160 rejected under 35 U.S.C. 103(a) as being unpatentable over **newly cited** Mignot et al in view of Cheesebeuf et al, Parenteau et al and **new cited** Cleveland et al.

Claims are drawn to a method of cultivating a mammalian cell comprising obtaining a mammalian cell and contacting the cell with a serum free and protein free or basal culture medium containing polysulfonated polyanionic compounds or polycationic compounds. The medium can have a IX or 10X medium formulation, can contain amino acids such as L-alanine, and various other ingredients, and supplements such as heparin and organic peptides, vitamins such as biotin, salts such as calcium. The cell types can be of epithelial (normal or abnormal such as a transformed cell) and of human origin. The serum free can be free of animal derived components. Further a method of replacing protein in a mammalian cell culture medium is claimed which comprises eliminating insulin and transferrin and replacing them with zinc and iron in the medium. The medium may not contain dextran sulfate.

Mignot et al is discussed above.

Cheesebeuf et al teach basal medium for culturing animal cells and can be devoid of animal derived components such as hormones and growth factors, note col. 2, lines 35-40 and col. 3 lines 20-25, 45-46.

Parenteau et al teach a method of culturing a mammalian cell in a culture medium using IX formulation mediums that iron can be used in place of transferrin, note col. 5, line 28.

Cleveland et al teach a protein free culture medium for culturing mammalian cells wherein the elimination of albumin, transferrin and insulin is an important advance in mammalian cell culture media. Note col. 3, lines 35-40 and 55-69.

The claims differ from Mignot et al in that certain claimed features are not disclosed such as components of culture media, IX formula media, elimination of transferrin and insulin, etc.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of Mignot et al, Cheesbeuf et al, Parenteau et al and Cleveland et al to obtain a mammalian cell and contacting said cell with a basal serum free, protein free, non-animal derived cell culture medium containing IX formulation ingredients and to replace transferrin with iron and insulin with zinc, therein. Further to concentrate the medium formulation to a 10X concentrated medium formulation is well with the purview of an ordinary artisan. Each of the ingredients and supplements are disclosed by the cited prior art. To select for organic peptides such as soy peptides is also an obvious modification of the cited prior art. As well, the salt

ingredient is disclosed by the cited prior art. To omit dextran sulfate or to include is also well within the teachings of the cited prior art as discussed above. Various mammalian cell types are further disclosed, some of which are abnormal or transformed cells. One of skill in the art would have been motivated by the prior art to cultivate mammalian cells by contacting them with these well known ingredients in culture medium as disclosed by the prior art. No unexpected successful results have been obtained. Therefore, in the absence of persuasive evidence to the contrary the claims are deemed *prima facie* obvious over the cited prior art.

Claims 33-34, 73-77 and 161-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over **newly cited** Mignot et al in view of Cheesebeuf et al, Parenteau et al and **new cited** Cleveland et al. as applied to claims above, and further in view of **newly cited** Wang et al.

Claims are discussed above and are further drawn to culturing human cells selected from 293 embryonic kidney cells and method of producing a virus which includes the method steps as discussed above but also contacting cell with a virus to promote viral infection of the cell wherein the virus can be an adeno-assoicated virus and further method of cultivating 293 cells wherein the polysulfonated or polysulfated compound is dextran sulfate.

Each of Mignot et al in view of Cheesebeuf et al, Parenteau et al and **new cited** Cleveland et al are discussed above.

Wang et al teach 293 cells and method of producing a virus which includes contacting cells with a virus to promote viral infection of the cell wherein the cell can be an adeno-associated virus. Note col. 16, lines 53-54 and col. 19, line 5.

The claims differ from Mignot as discussed above.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to cultivate cells as discussed above and further to cultivate 293 cells and produce a virus as disclosed by Wang et al under conditions disclosed by the cited prior art discussed above. Clearly one of skill would have been motivated to select for 293 cells which would have been a choice of functional equivalents available to the artisan. One of skill would have expected successful results and would have been motivated to produce a virus using the conditions of Mignot et al in view of Cheesebeuf et al, Parenteau et al and **newly cited** Cleveland et al., especially since Wang et al teach the same. Each of the claim features are disclosed or suggested by the cited prior art and are discussed above. Wang et al clearly teach any missing deficiencies of the cited prior art such as 293 cells and production of a virus via the step of contacting the cells with a virus. Further, the prior art does recognize that dextran sulfate can be used especially to prevent cell clumping. In the absence of unexpected successful results the claims are rendered *prima facie* obvious over the cited prior art.

Claims 15-17, 20-21 and 154 are considered to be free of the cited prior art and would be allowable if claim 15 is amended in line 3 by inserting –serum free or protein free-- before “chemically” and in line 11 by canceling “or polycationic” and inserting --

selected from the group consisting of a polysulfonated compound and a polysulfated compound-- after “compound” .

All art-rejected claims fail to be patentably distinguishable over the state of the art discussed above and cited on the enclosed PTO-892 and/or PTO-1449. Therefore, these claims are properly rejected.

The remaining references listed on the enclosed PTO-892 and/or PTO-1449 are cited to further show the state of the art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah K. Ware whose telephone number is 571-272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah K. Ware
March 20, 2004

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1651